Title: Antioxidant And Radical...
Inventor: Raymond J. Bergeron, Jr.

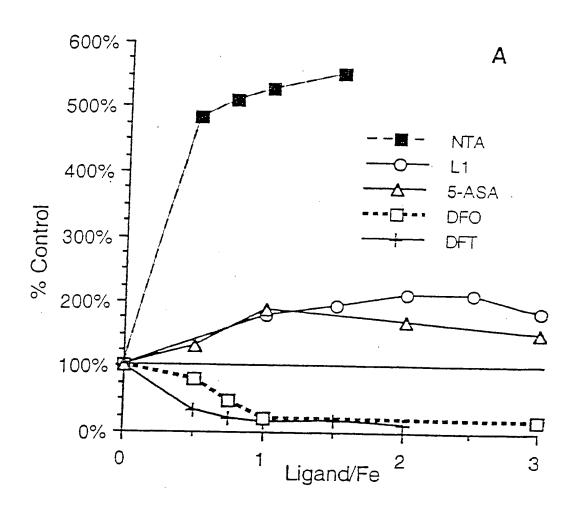


FIG. 1A

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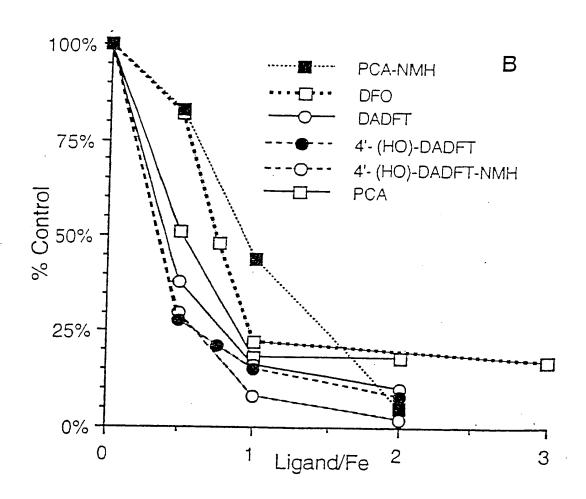


FIG. 1B

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Control

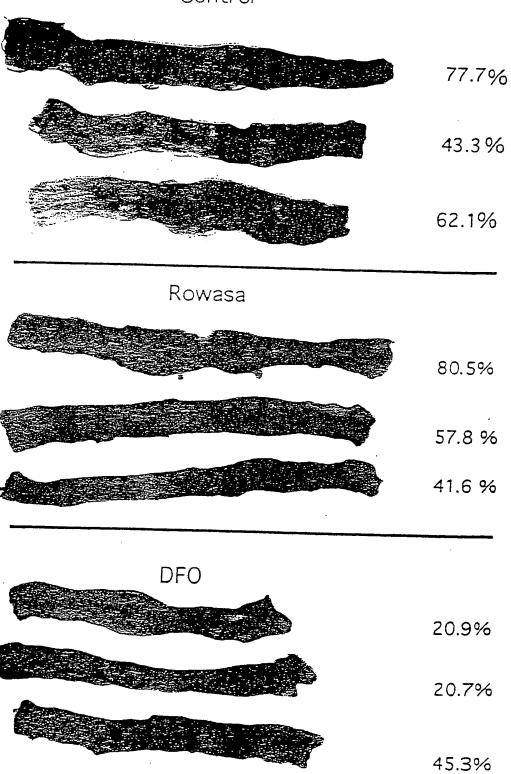


FIG. 2

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FIG. 3

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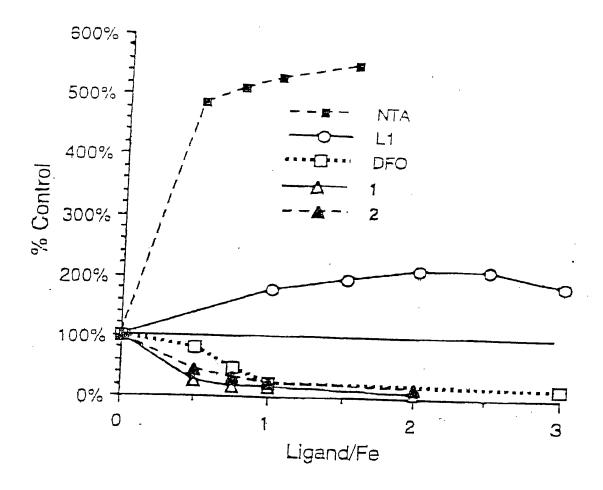


FIG. 4

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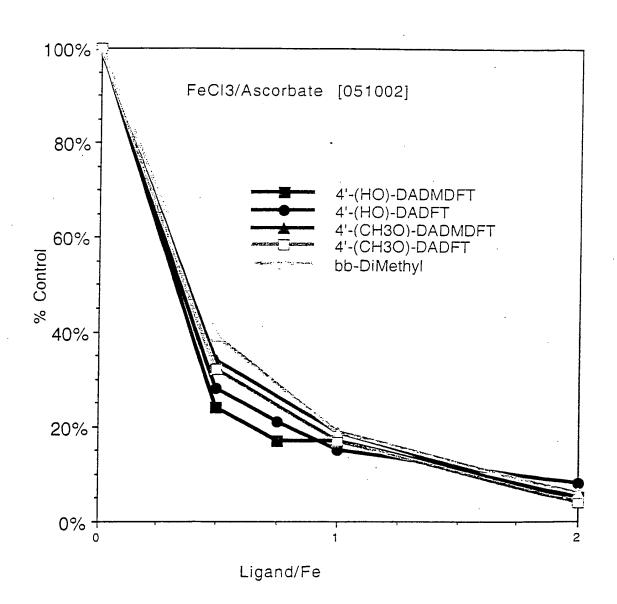


FIG. 5

11tle.
Inventor:

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Compound	Slope x 10 ³ OD units/µM*
DFT	-0.9
DMDFT	-1.3
PCA	-3.3
DADFT	-25.1
DADMDFT	-28.1
5-ASA	-34.4
PCA-NMH	-34.6
Trolox	-36.6
DMDFT-NMH	-47.4
L1	-52.9
4'-(HO)-DADMDFT	-101.6
4'-(HO)-DADFT	-105.6
4'-(HO)-DADMDFT-NMH	-135.5
DFO	-136.8
4'-(HO)-DADFT-NMH	-141.4

^{*}The slope was derived from A_{734} vs time data over a six-minute reaction period between the chelator of interest and the 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation (ABTS $^{-+}$), which was formed from the reaction between ABTS and persulfate. A negative slope represents a decrease in the amount of highly colored radical cation over the time interval. Trolox, an analog of Vitamin E, served as a positive control.

litle:

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Inventor:

Damage P vs P vs MPO. P vs P vs Compound* N (%) Ť control‡ parent§ controlf parents activity \ N/A** Control (no acid) 10 4 ± 5 < 0.001 **4494** ± **2254** < 0.001 N/A Control 4% acetic acid 65 = 1813 N/A N/A 91479 = 84927 ΝiΑ N/A DMDFT-NMH 10 22 = 17< 0.001 < 0.001 14406 ± 8683 < 0.005 10.0> DMDFT 10 61 ± 15 N.S. †† N/A 39229 ± 27109 < 0.05 N/A (DMDFT-NMH),/Fe 9 45 ± 24 <0.05 <0.02** 54370 ± 18749 N.S. <0.001‡‡ PCA 10 44 ± 11 < 0.001 N/A 29942 ± 11255 < 0.02 N/A PCA-NMH 9 38 = 18< 0.002 N.S. 23642 ± 14341 < 0.01 N.S. 4'-(HO)-DADMDFT 57 = 1510 N.S. N/A 56466 ± 52617 N.S. N/A 4'-(HQ)-DADMDFT-NMH 39 ± 11 10 < 0.001 < 0.005 18426 ± 20930 < 0.005 <0.05 DFO 9 39 ± 15 < 0.001 N/A 20049 = 17314< 0.01 N/A 4'-(HO)-DADFT 62 = 10N.S. N/A 64192 = 30802N.S. N/A 4'-(HO)-DADFT-NMH 46 = 23<0.05 8 =0.05 41021 = 35525<0.05 N.S.

N/A

51805 = 38165

N/A

Rowasa®§§

62 = 19

N.S.

^{*}All chelators (2 ml) were administered intracolonically at a dose of 650 µmol kg⁻¹. Rowasa® (2 ml, 66.7 mg ml⁻¹ 5-ASA) was given intracolonically at a dose of 2318 µmol kg⁻¹.

[†]Percent damage in scanned images of the colons was measured with the aid of the Adobe Photoshop program; the mean percentage of the image scored as "damaged" (as detailed in the Experimental Section) ± standard deviation is reported.

[‡]P versus 4% acetic acid control animals.

 $[\]delta P$ versus animals treated with the respective carboxylic acid.

[¶] Myeloperoxidase (MPO) activity expressed as mAU min¹ g of colonic tissue¹, mean ± standard deviation.

^{**}N/A, not applicable.

^{††}N.S., not significant (P > 0.05)

[‡]IIn this instance, P versus animals treated with free, uncomplexed DMDFT-N.

^{§§}The pharmaceutical preparation, which contains 5-ASA (66.7 mg ml⁻¹), was tested in the rodents.

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Compound	slope x 10 ³ OD units/μM ^a
Trolox	-37°
L1	-53 ^b
4'-(OH)-DADMDFT	-102 ^b
BDU	-136
DFO	-137 ^b

^a The slope was derived from A_{734} vs time data over a 6-min reaction period between the chelator of interest and the 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation (ABTS⁻), which was formed from the reaction between ABTS and persulfate. A negative slope represents a decrease in the amount of highly colored radical cation over the time interval. Trolox, an analogue of vitamin E, served as a positive control.

^b Bergeron, R.J.; Wiegand, J.; Weimar, W.R.; Nguyen, J.N.; Sninsky, C.A., unpublished results.

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compound	slope × 10 ³ OD units/µM"
4'-(CH;O)-DADMDFT	-33
4'-(CH ₃ O)-DADFT	-36
Trolox	- 37 [.]
β,β-Dimethyl	-7 0
4'-(HO)-DADMDFT	-102
4'-(HO)-DADFT	-106

^a The slope was derived from A_{734} vs time data over a 6-min reaction period between the chelator of interest and the 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation (ABTS'*), which was formed from the reaction between ABTS and persulfate. A negative slope represents a decrease in the amount of highly colored radical cation over the time interval from an initial OD₄₇₀ of 1.000. Trolox, an analogue of vitamin E, served as a positive control.